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(54) Title: **HEPATITIS C VIRAL-LIKE PARTICLE PURIFICATION**

(57) **Abstract:** Methods for obtaining HCV complexes and HCV-like particles comprising HCV structural genes are provided. In one method, cells containing HCV-like particles are lysed with digitonin in the presence of protease inhibitors. Polyethylene glycol is slowly added to the lysate, to provide a precipitate that comprises complexes of the HCV structural proteins associated with lipid vesicles or micelles and complexes comprising viral structural proteins in the form of insoluble aggregates. In another method, the lysate is centrifuged through a sucrose cushion. Preferably, the pellet is then subjected to equilibrium ultracentrifugation, to provide a preparation of HCV-like particles that are heterogenous in size. The third method comprises subjecting the infected cells to hypertonic/hypotonic shock, and lysing the cells with digitonin in the presence of protease inhibitors. The lysate is pelleted and fractionated to provide a population of HCV-like particles that are substantially homogenous and have an average diameter of about 50 nm. As used herein the term "substantially homogenous" means that the shape of the particles are similar and that the size of the particles vary by 10% or less. Methods of using the HCV complexes and HCV-like particles as screening tools, diagnostic tools, and immunogenic compositions are also provided. Methods of treating patients exhibiting symptoms of HCV infection with compounds or substances that interfere with binding or internalization of the present HCV-like particles to asialoglycoprotein receptors are also provided.

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**INTERNATIONAL SEARCH REPORT**

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**A. CLASSIFICATION OF SUBJECT MATTER**

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US CL : 435/235.1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 435/235.1, 70.1; 530/387; 424/130.1; C12N 7/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
PubMed

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE. S. Improved detection of antibodies to hepatitis C virus using a second generation ELISA Adv. Exp. Biol. 1992, Abstract	15
Y	US 5,905,040 (MAZZARA et al.) 18 June 1999 (18.06.1999), Abstract, column 22, lines 27-50	1-14, 16-22
Y	GROSE. C. Purification and molecular anatomy of the varicella-zoster virion Biken J. March 1983, Vol. 26, No. 1, Abstract	1-4
Y	CHIBA. J. Serodiagnosis of hepatitis C virus (HCV) infection with an HCV core protein molecularly expressed by a recombinant baculovirus Proc. Natl. Acad. Sci U S A June 1991, Vol. 88, Abstract	1-8, 16-22
Y	US 5,420,026 A (PAYNE) 30 May 1995 (30.05.1995), Abstract, column 9, lines 44-67, column 10, lines 1-39	5-14, 16-22
Y	US 5,359,046 A (CAPON et al.) 25 October 1994 (25.10.1994), column 15, lines 16-37	3, 7, 11
Y	US 5,591,595 A (AKEN et al.) 07 January 1997 (07.01.1997), column 8, lines 48-65	9-14
Y	WO 92/08734 (CHIRON CORP.) 29 May 1992 (29.05.1992) Abstract, page 2, lines 23-29, page 3, lines 1-6	12, 13, 20, 21

Further documents are listed in the continuation of Box C.  See patent family annex.

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Name and mailing address of the ISA/US  Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer  Tim Brown  Telephone No. (571) 272-1600

## INTERNATIONAL SEARCH REPORT

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,679,342 A (HOUGHTON et al.) 21 October 1997 (21.10.1997), Abstract, column 11, lines 29-40	18, 19